

Appl. No. 09/350,202

Amdt. dated September 22, 2004

Second Suppl. Amdt. and Response to Office Action of April 13, 2004.

Listing of Pending Claims:

Claims 1-59. (Cancelled)

Claim 60. (Currently Amended): A method for inducing *ex vivo* proliferation of a population of T cells to sufficient numbers for use in therapy, comprising contacting a population of T cells *ex vivo* with a surface having covalently attached thereto:

- (a) an anti-CD3 antibody or CD3-binding fragment thereof, which provides a primary activation signal to the T cells, thereby activating the T cells; and
- (b) an anti-CD28 antibody or CD28-binding fragment thereof, which stimulates a CD28 accessory molecule on the surface of the T cells, thereby stimulating the activated T cells, wherein the anti-CD3 antibody or CD3-binding fragment thereof and the anti-CD28 antibody or CD28-binding fragment thereof are covalently attached to the same surface, the anti-CD3 antibody or CD3-binding fragment thereof and the anti-CD28 antibody or CD28-binding fragment thereof thereby inducing the population of T cells to proliferate to sufficient numbers for use in therapy.

Claim 61. (Currently Amended): The method of claim 60, wherein the anti-CD3 antibody or CD3-binding fragment thereof is an anti-human CD3 monoclonal antibody or CD3-binding fragment thereof.

Claim 62. (Currently Amended): The method of claim 60, wherein the anti-CD28 antibody or CD28-binding fragment thereof is an anti-human CD28 monoclonal antibody or CD28-binding fragment thereof.

Claim 63. (Currently Amended): The method of claim 60, wherein the anti-CD3 antibody or CD3-binding fragment thereof and the anti-CD28 antibody or CD28-binding fragment thereof, are covalently attached to the same surface using tosyl linkage.

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Claim 64. (Currently Amended): The method of claim 60, further comprising:
monitoring the proliferation of the T cells; and
reactivating and re-stimulating the T cells with the the anti-CD3 antibody or CD3-binding fragment thereof and the anti-CD28 antibody or CD28-binding fragment thereof when the rate of T cell proliferation has decreased to induce further proliferation of the T cells.

Claim 65. (Previously Presented): The method of claim 64, wherein the step of monitoring proliferation of the T cells is by examining cell size or determining the level of expression of a cell surface molecule selected from the group consisting of B7-1, B7-2 and any combination thereof, and the step of reactivating and restimulating is initiated when T cell size has decreased or when the level of the cell surface molecule has decreased.

Claim 66. (Cancelled)

Claim 67. (Previously Presented): The method of claim 60, wherein the T cells are induced to proliferate to about 100-fold the original T cell population.

Claim 68. (Previously Presented): The method of claim 60, wherein the T cells are induced to proliferate to about 100,000-fold the original T cell population.

Claim 69. (Previously Presented): The method of claim 60, wherein the T cells are induced to proliferate for at least 3 days.

Claim 70. (Previously Presented): The method of claim 60, wherein the T cells are induced to proliferate for at least 7 days.

Claim 71. (Previously Presented): The method of claim 60, wherein the surface is a bead.

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Claim 72. (Previously Presented): The method of claim 70, wherein the bead is a magnetic bead.

Claim 73. (Previously Presented): The method of claim 70, wherein the bead is a polystyrene bead.

Claim 74. (Previously Presented): The method of claim 60, wherein the surface is a cell surface.

Claim 75. (Previously Presented): The method of claim 60, wherein the surface is a tissue culture dish.

Claim 76. (Previously Presented): The method of claim 60, wherein the population of T cells are induced to proliferate to sufficient numbers for use in treating cancer.

Claim 77. (Previously Presented): The method of claim 60, wherein the population of T cells are induced to proliferate to sufficient numbers for use in treating an infectious disease.

Claim 78. (Previously Presented): The anti-CD28 antibody of claim 62, wherein the antibody is 9.3 produced by the hybridoma assigned ATCC No. HB-10271.

Claim 79. (Previously Presented): The anti-CD28 antibody of claim 62, wherein the antibody is EX 5.3D10 produced by the hybridoma assigned ATCC No. HB-11373.